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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/581,366	00/00/00	RESZKA	R 2936.169/00

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NORRIS, MCLAUGHLIN & MARCUS P.A
220 EAST 42ND STREET
30TH FLOOR
NEW YORK NY 10017

EXAMINER	
SCHMIDT,M	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 05/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/581,366	RESZKA, REGINA	
	Examiner	Art Unit	
	Mary Schmidt	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Specification

1. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(I) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

2. The disclosure is objected to because of the following informalities: The specification as filed contains Drawings, but no Brief Description of the Drawings.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In general, due the translation of the claims from German into English, several errors appear in the claims. Claims 2-14, 19 and 22 also have lists of limitations which appear to be improper Markush groupings. Claims 3, 5, 6, 8, 10, 11, 13, 14, 15, 17, 18, 20, 21, 22, 23 and 24 all claim "one of the claims..." in the preamble although the claims only depend from one claim as amended.

Claims 1 and 22 are indefinite because the claims contain bullets. It is suggested that either numbers (1, 2, 3) or letters (a, b, c) are used to define the groups instead. (And said nomenclature is kept consistent throughout the claims.)

Regarding claims 1, 3, 4, 11, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 3 contains typographical errors. For instance, "antiangiogenesis" and "apoptose" are misspelled.

In claim 4, "the proteins" lacks antecedent basis.

In claim 5, "the suicide genes" and "the cytokine genes" lack antecedent basis. Further, "cytokinin" is misspelled and it is unclear what is claimed with the use of the terminology "and/or" prior to the list of interleukin genes.

In claim 6, "the water or lipid soluble genetic material" lacks antecedent basis. Further, the use of the terminology "and/or" does not provide a clear picture of what the structure, the metes and bounds, of the claimed invention is.

In claim 7, the use of the term "preferably" is unclear since the metes and bounds of the molar ratio is unclear.

In claim 11, the terminology "the enzyme of a sphingolipid" is unclear since it is not clear what is meant by this phrase.

In claims 13 and 19: The use of the trademarks Poloxamer, Iopromide, Ioxitalamate, Ioxaglate, Iopamidol, Iohexol, Iotralon, Metrizamide, and Ultravis have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claims 23-24 are incomplete since they do not contain a final step which relates back to the preamble. Further, they lack antecedent basis for the language "the therapeutically."

5. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-22 are drawn to pharmaceutical compositions comprising a broad scope of any genetic material, not encapsulated or encapsulated in PEG-, immuno-, immuno/PEG-, cationic, optionally polymer-modified liposomes, lyophilized or degradable starch particles and/or gelatin and/or polymer particles, such as nanoparticles and iodine-, gadolinium-, magnetite-or fluorine-containing contrasting agents. The broad claim (1) is interpreted to need all of the claimed limitations, but in view of the 35 U.S.C. 112, second paragraph, rejections above, the metes and bounds of the claimed invention are not entirely clear.

The liposome art is replete with examples of making liposomes for delivery of genetic materials to cells in culture and *in vivo*, but the field of gene therapy does not generally teach one such liposome which is effective for the delivery of any genetic material, thus providing a general guidance for delivery of any genetic material via liposomes for gene therapeutic purposes. The specification as filed must teach how to make and use the claimed invention such that one skilled in the art would not need to practice undue experimentation to make and use the invention as claimed.

In view of the 35 U.S.C. 112, 2nd paragraph, rejections above, the exact scope of the claimed invention is not clear as the claims are presently written. The implied use of any pharmaceutical composition is for therapeutic purposes. The specification teaches by way of example administration of "pUT649 to tumor-carrying rats and a statistically significant decrease in the liver metastases in comparison to the control group" (Example 2). It is not clear from this example how the administration of the pUT649 to the tumor-carrying rats correlates to making any liposomal composition encompassing any genetic material for administration as a therapeutic agent to any whole organism as implied by the claim to the pharmaceutical compositions. The usefulness of a pharmaceutical composition relies on the active ingredient, in this case the gene therapeutic component to have a therapeutic use.

There is a high level of unpredictability in the gene therapeutic art for design and administration of gene therapeutic constructs to cells in whole organisms. Note Anderson who teaches the unpredictability in the art for design of gene therapeutic vectors: "The problems that investigators face in developing retroviral vectors that are effective in treating disease are of four main types: obtaining efficient delivery, transducing non-dividing cells, sustaining long-term gene expression, and developing a cost-effective way to manufacture the vector" (p. 25, col. 2, second para.). Note also Reynolds et al. who further teach the difficulties with vector design in the field of gene therapy (see Table 1 for instance). Although the field of gene therapy benefits from optimization of delivery by improvement of liposomal compositions, the active ingredient of the claimed pharmaceutical compositions remains the gene therapeutic agent. As such, with the high

level of unpredictability in the art for design of such constructs, one skilled in the art would necessarily practice "trial and error experimentation" to make and use the invention as broadly claimed to design genetic therapeutic constructs for use as pharmaceutical compositions having implied therapeutic use. The specific factors considered unpredictable are the (1) design of the genetic constructs for expression of any therapeutic gene as broadly claimed, (2) routes of administration, (3) sustained expression for therapeutic purposes, (4) expression in the specific cells of interest, and (5) dosage and toxicity.

In view of the lack of general guidance in either the specification or the art for successful design of any pharmaceutical composition as broadly claimed for expression of any gene therapeutic agent in any whole organism, one skilled in the art would necessarily practice undue experimentation to make and use the invention as broadly claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
May 7, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER